# Survival of chemoresistant cancer cells exposed to x-rays and heavy ions

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## Introduction

Cancer stem-cells (CSCs) are more resistant to most conventional therapy than differentiated tumor cells. A rapid relapse after treatment can occur, caused by CSCs which were not eliminated by the applied therapy [1]. CSCs are supposed to be radioresistant and/or chemoresistant. Culturing cancer cells in the presence of a low dose of a chemotherapeutic agent is one of the methods to enrich CSCs. In this study, etoposide is used to enrich CSCs in glioblastoma and neuroblastoma cell lines. Etoposide is a topoisomerase inhibitor and causes errors in DNA synthesis and promotes apoptosis of cancer cells. It is used as a form of chemotherapy for cancers such as glioblastoma multiforme.

In this report, the survival of chemoresistant cancer cells is shown compared with original ones exposed to x-rays and heavy ions. All cell lines in the report are kindly given by Dr. D. Diaz-Carballo, Marienhospital Herne, Klinikum der Ruhr-Universität Bochum, Bochum, Germany.

## Material and Methods

Four cell lines (LAN-1 WT, LAN-1 RETO, ASTRO WT, ASTRO RETO) derived from human tumor tissue of patients are cultured in DMEM medium, supplemented with 10% fetal calf serum (FCS) and 1% Penicillin/Streptomycin, and kept in a humidified atmosphere of 5% $CO_2$ at 37°C. All cells show adherent growth. ASTRO cell lines are derived from glioblastoma multiforme and LAN-1 cell lines are derived from neuroblastoma. RETO cells are cultured in Medium containing 4µg/ml etoposide. Carbon ion irradiation was performed using a 1cm extended Bragg peak at a dose-averaged LET of 100 keV/µm. X-ray irradiation was performed using 250 kVp. Cell survival was measured with a colony formation assay.

## Results

The survival curves show that carbon ion irradiation is more effective than x-ray in all four cell lines (figure 1, figure 2). For LAN-1 cells, RETO cells (cultured in the presence of etoposide) are more resistant than WT cells (cultured without etoposide) after x-ray and carbon ion irradiation (figure 1), but for ASTRO cells, RETO cells (cultured with etoposide) are more sensitive than WT cells (cultured without etoposide) after x-ray and carbon ion irradiation (figure 2).

## Conclusions

Carbon ion irradiation is more effective than x-ray for both untreated cancer cell lines and chemoresistant cell lines. For LAN-1 cells, chemoresistant cells (RETO) are more radioresistant than untreated cells (WT), while this effect was not found in ASTRO cells.

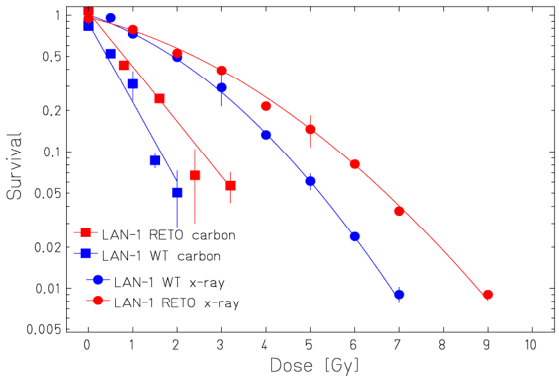


Figure 1: Survival of LAN-1 WT and LAN-1 RETO cells irradiated by x-ray and carbon ions.

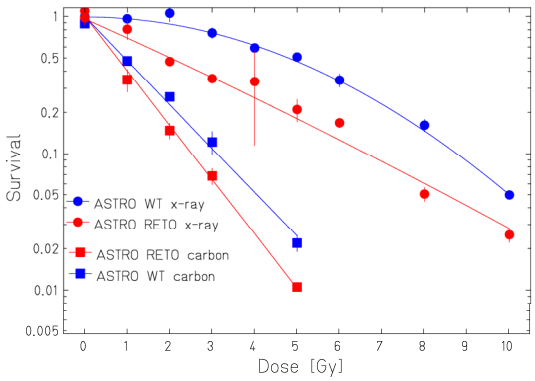


Figure 2: Survival of ASTRO WT and ASTRO RETO cells irradiated by x-ray and carbon ions.

## References

[1] L. Vermeulen et al. "The developing cancer stem-cell model: clinical challenges and opportunities." *Lancet Oncol*, February 2012, 13(2), p.e83-89